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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  May 12   EXTEND option available in structure searching
 NEWS  4  May 12   Polymer links for the POLYLINK command completed in REGISTRY
 NEWS  5  May 27   New UPM (Update Code Maximum) field for more efficient patent
                   SDIs in CAplus
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 NEWS  7  Jun 22   STN Patent Forums to be held July 19-22, 2004
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 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
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               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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=> s (RAR antagonist)
L1          289 (RAR ANTAGONIST)

=> s l1 and (BMP? or (osteogenic protein) or OPS or cytokine#)
L2           29 L1 AND (BMP? OR (OSTEOGENIC PROTEIN) OR OPS OR CYTOKINE#)

=> s l2 and (chondrogen?)
L3            8 L2 AND (CHONDROGEN?)

=> s l3 and (solution or suspension or gel or matirx or cream or gel or film or
paste or capsule or pill or tablet or encapsul? or Microcapsule# or micropart?)
   4 FILES SEARCHED...
L4            3 L3 AND (SOLUTION OR SUSPENSION OR GEL OR MATIRX OR CREAM OR
                GEL OR FILM OR PASTE OR CAPSULE OR PILL OR TABLET OR ENCAPSUL?
                OR MICROCAPSULE# OR MICROPART?)

=> s l4 and liposom?
L5            3 L4 AND LIPOSOM?

=> d l5 1-3 ibib abs

L5   ANSWER 1 OF 3  USPATFULL on STN
ACCESSION NUMBER:        2003:181419  USPATFULL
TITLE:                   Compositions and methods for affecting osteogenesis
INVENTOR(S):             Underhill, T. Michael, Ontario, CANADA
                         Sampaio, Arthur V., Ontario, CANADA
                         Weston, Andrea D., Ontario, CANADA

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2003125252      A1   20030703
APPLICATION INFO.:       US 2002-221602     A1   20020912  (10)
                         WO 2001-CA317           20010313
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH,
                         NC, 27627
NUMBER OF CLAIMS:        72
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      6 Drawing Page(s)
LINE COUNT:              1833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The invention relates to compositions for promoting and inhibiting
       osteogenesis and to methods for treating bone abnormalities resulting
       from injury, toxicity or disease and for ex vivo bone tissue
       engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

L5 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER:	2003:47877 USPATFULL
TITLE:	Use of ligands for treatment of diseases responsive to retinoids
INVENTOR(S):	Chambon, Pierre, Blaesheim, FRANCE Borrelli, Emiliana, Strasbourg, FRANCE Ghyselinck, Norbert B., Strasbourg, FRANCE Dupe, Valerie, London, UNITED KINGDOM Mark, Manuel, Morchwiller, FRANCE Metzger, Daniel, Strasbourg, FRANCE
PATENT ASSIGNEE(S):	Institut National de la Santa et de la Recherche Medicale, Paris, FRANCE (non-U.S. corporation) Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation) Universite Louis Pasteur, Strasbourg, FRANCE (non-U.S. corporation) Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6521814	B1	20030218
APPLICATION INFO.:	US 1998-218446		19981222 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-68471P	19971222 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Reynolds, Deborah J.
ASSISTANT EXAMINER:	Sorbello, Eleanor
LEGAL REPRESENTATIVE:	Sterne, Kessler Goldstein & Fox
NUMBER OF CLAIMS:	73
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	124 Drawing Figure(s); 51 Drawing Page(s)
LINE COUNT:	5178

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods for treatment of neurological disease by administering an agent which interacts with a retinoid receptor associated with the neurological disease. The invention is also related to a method of modulating dopamine receptor synthesis by introducing an agent that interacts with a retinoid receptor associated with the dopamine receptor synthesis. The invention is further related to a transgenic animal, e.g., mouse, and mammalian cell line, which is deficient in the normal synthesis of one or more receptors of RARα, β, γ and RXR, and cell line thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 3 EUROPATFULL COPYRIGHT 2004 WILA on STN

GRANTED PATENT - ERTEILTES PATENT - BREVET DELIVRE

ACCESSION NUMBER:	1131067 EUROPATFULL EW 200420 FS PS
TITLE:	COMPOSITION AND USE OF RAR ANTAGONISTS FOR PROMOTING **CHONDROGENESIS**. ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE**. COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE**.
INVENTOR(S):	UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA; WESTON, Andrea, Dawn, Univ.of Western Ontario, The

	Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA
PATENT ASSIGNEE(S):	The University of Western Ontario, Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA
PATENT ASSIGNEE NO:	1820961
AGENT:	Holliday, Louise Caroline, D Young & Co, 21 New Fetter Lane, London EC4A 1DA, GB
AGENT NUMBER:	95451
OTHER SOURCE:	MEPB2004021 EP 1131067 B1 0035
SOURCE:	Wila-EPS-2004-H20-T1
DOCUMENT TYPE:	Patent
LANGUAGE:	Anmeldung in Englisch; Veroeffentlichung in Englisch
DESIGNATED STATES:	R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE; R AL; R LT; R LV; R MK; R RO; R SI
PATENT INFO.PUB.TYPE:	EPB1 EUROPAEISCHE PATENTSCHRIFT (Internationale Anmeldung)

PATENT INFORMATION:

PATENT NO	KIND	DATE
EP 1131067	B1	20040512
'OFFENLEGUNGS' DATE:		20010912
APPLICATION INFO.:	EP 1999-955613	19991119
PRIORITY APPLN. INFO.:	CA 1998-2254429	19981119
RELATED DOC. INFO.:	WO 99-CA1106	991119 INTAKZ
	WO 2000030635	000602 INTPNR
REFERENCE PAT. INFO.:	WO 98-08546 A	WO 99-24415 A
	US 5827500 A	

REF. NON-PATENT-LIT.: KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91., XP000879298 PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP10114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06) STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8., XP000879170 KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY., XP000879148 NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62., XP000653320 JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

=> d l3 1-8 ibib abs

L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:368088 CAPLUS
DOCUMENT NUMBER: 133:828
TITLE: Composition and use of RAR antagonists for promoting **chondrogenesis**
INVENTOR(S): Underhill, Tully Michael; Weston, Andrea Dawn
PATENT ASSIGNEE(S): The University of Western Ontario, Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000030635	A1	20000602	WO 1999-CA1106	19991119
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1131067	A1	20010912	EP 1999-955613	19991119
EP 1131067	B1	20040512		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002530331	T2	20020917	JP 2000-583518	19991119
AU 764394	B2	20030814	AU 2000-12552	19991119
AU 2000012552	A5	20000613		
US 2002061514	A1	20020523	US 2001-957456	20010921

PRIORITY APPLN. INFO.:
CA 1998-2254429 A 19981119
WO 1999-CA1106 W 19991119
US 2000-234242P P 20000921

AB The invention provides compns. comprising a **RAR antagonist** for promoting **chondrogenesis**, as well as methods employing such compns. for treating cartilage and associated bone abnormalities resulting from injury or disease and for ex vivo tissue engineering.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:147914 CAPLUS
DOCUMENT NUMBER: 132:261066
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine & Dentistry, The University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Journal of Cell Biology (2000), 148(4), 679-690
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The generation of the paraxial skeleton requires that commitment and

differentiation of skeletal progenitors is precisely coordinated during limb out-growth. Several signaling mols. have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects. Further anal. of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2003:181419 USPATFULL

TITLE: Compositions and methods for affecting osteogenesis

INVENTOR(S): Underhill, T. Michael, Ontario, CANADA
Sampaio, Arthur V., Ontario, CANADA
Weston, Andrea D., Ontario, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003125252	A1	20030703	
APPLICATION INFO.:	US 2002-221602	A1	20020912	(10)
	WO 2001-CA317		20010313	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 72
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to compositions for promoting and inhibiting osteogenesis and to methods for treating bone abnormalities resulting from injury, toxicity or disease and for ex vivo bone tissue engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2003:47877 USPATFULL

TITLE: Use of ligands for treatment of diseases responsive to retinoids

INVENTOR(S): Chambon, Pierre, Blaesheim, FRANCE
Borrelli, Emiliana, Strasbourg, FRANCE
Ghyselinck, Norbert B., Strasbourg, FRANCE
Dupe, Valerie, London, UNITED KINGDOM
Mark, Manuel, Morchwiller, FRANCE

	Metzger, Daniel, Strasbourg, FRANCE
PATENT ASSIGNEE(S):	Institut National de la Santa et de la Recherche Medicale, Paris, FRANCE (non-U.S. corporation) Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation) Universite Louis Pasteur, Strasbourg, FRANCE (non-U.S. corporation) Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6521814	B1	20030218	
APPLICATION INFO.:	US 1998-218446		19981222	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-68471P	19971222	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Reynolds, Deborah J.
ASSISTANT EXAMINER:	Sorbello, Eleanor
LEGAL REPRESENTATIVE:	Sterne, Kessler Goldstein & Fox
NUMBER OF CLAIMS:	73
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	124 Drawing Figure(s); 51 Drawing Page(s)
LINE COUNT:	5178

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods for treatment of neurological disease by administering an agent which interacts with a retinoid receptor associated with the neurological disease. The invention is also related to a method of modulating dopamine receptor synthesis by introducing an agent that interacts with a retinoid receptor associated with the dopamine receptor synthesis. The invention is further related to a transgenic animal, e.g., mouse, and mammalian cell line, which is deficient in the normal synthesis of one or more receptors of RARα, β, γ and RXR, and cell line thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 8 EUROPATFULL COPYRIGHT 2004 WILA on STN

GRANTED PATENT - ERTEILTES PATENT - BREVET DELIVRE

ACCESSION NUMBER:	1131067 EUROPATFULL EW 200420 FS PS
TITLE:	COMPOSITION AND USE OF RAR ANTAGONISTS FOR PROMOTING **CHONDROGENESIS**. ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE**. COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE**.
INVENTOR(S):	UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA; WESTON, Andrea, Dawn, Univ.of Western Ontario, The Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA
PATENT ASSIGNEE(S):	The University of Western Ontario, Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA
PATENT ASSIGNEE NO:	1820961
AGENT:	Holliday, Louise Caroline, D Young & Co, 21 New Fetter Lane, London EC4A 1DA, GB
AGENT NUMBER:	95451

OTHER SOURCE: MEPB2004021 EP 1131067 B1 0035
SOURCE: Wila-EPS-2004-H20-T1
DOCUMENT TYPE: Patent
LANGUAGE: Anmeldung in Englisch; Veroeffentlichung in Englisch
DESIGNATED STATES: R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE; R AL; R LT; R LV; R MK; R RO; R SI
PATENT INFO.PUB.TYPE: EPB1 EUROPAEISCHE PATENTSCHRIFT (Internationale Anmeldung)
PATENT INFORMATION:

PATENT NO	KIND	DATE
EP 1131067	B1	20040512
'OFFENLEGUNGS' DATE:		20010912
APPLICATION INFO.: EP 1999-955613		19991119
PRIORITY APPLN. INFO.: CA 1998-2254429		19981119
RELATED DOC. INFO.: WO 99-CA1106		991119 INTAKZ
WO 2000030635		000602 INTPNR
REFERENCE PAT. INFO.: WO 98-08546 A		WO 99-24415 A
US 5827500 A		

REF. NON-PATENT-LIT.: KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91., XP000879298 PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP10114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06) STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8., XP000879170 KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY., XP000879148 NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62., XP000653320 JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

L3 ANSWER 6 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2000153508 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10684250
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR: Weston A D; Rosen V; Chandraratna R A; Underhill T M
CORPORATE SOURCE: Division of Oral Biology, School of Dentistry, The University of Western Ontario, London, Ontario, Canada.
SOURCE: Journal of cell biology, (2000 Feb 21) 148 (4) 679-90. Journal code: 0375356. ISSN: 0021-9525.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000313

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L3 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:142678 BIOSIS
DOCUMENT NUMBER: PREV200000142678
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael [Reprint author]
CORPORATE SOURCE: School of Dentistry, Faculty of Medicine and Dentistry, University of Western Ontario, London, ON, N6A 5C1, Canada
SOURCE: Journal of Cell Biology, (Feb. 21, 2000) Vol. 148, No. 4, pp. 679-690. print.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Article
LANGUAGE: English
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AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation.

Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

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